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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/510,903	10/08/2004	Yasumichi Hitoshi	021044-003310US	1730

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EXAMINER	
NATARAJAN, MEERA	
ART UNIT	**PAPER NUMBER**
1609	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	04/02/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/510,903	HITOSHI ET AL.	
	Examiner	Art Unit	
	Meera Natarajan Ph.D.	1609	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 February 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-23 and 36-44* is/are pending in the application.

4a) Of the above claim(s) *1-22* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *23, 36-44* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *10/8/04* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Detailed Action

Election/Restrictions

1. Applicant's election with traverse of Group II and the Fanconi anemia group A protein (FANCA) election species in the reply filed on February 12, 2007 is acknowledged.

The traversal is on the ground(s) that Group I and Group II, both drawn to methods of identifying a compound that modulates cell cycle arrest, be examined together. Applicant also asserts that, at the very least, claim 1 is a genus claim as all method steps recited in claim 1 are found in claim 23. This is not found persuasive because the claims, as written, do not recite the same method steps. Claim 1 recites two steps; (i) contacting a *cell* comprising a target polypeptide and (ii) determining the chemical and phenotypic effect of the compound upon the cell comprising the target polypeptide or fragment thereof. Claim 23 recites two steps; (i) contacting the *compound* with a FANCA polypeptide and (ii) determining the physical effect of the compound upon the FANCA polypeptide. Step (ii) is different in claims 1 and 23, determining the "chemical and phenotypic effect" can involve different method steps than determining the "physical effect". The specifications of this application also disclose these two effects include separate methods and techniques (specifications p. 20, lines 29-32). The applicant discloses that "phenotypic or chemical effect" includes the ability to increase or decrease cellular proliferation, apoptosis, cell cycle arrest, or enzymatic activity and "physical effect" includes ligand binding or inhibition of ligand binding. The assays for testing compounds that modulate these activities differs in the

method objectives, method steps and parameters and in the reagents used. The requirement is still deemed proper and is therefore made FINAL.

2. Claims 1-22 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to non-elected inventions. Applicant timely traversed the restriction (election) requirement in the reply filed on February 12, 2007.

3. Claims 24-35 have been cancelled by applicant.

4. Claims 23 and 36-44 are under examination.

Objections

5. Claim 23 is objected to because of the following informalities: The claim recites, Fanconi anemia group A "protein polypeptide". The language is confusing since a polypeptide is a single linear chain of amino acids and a protein is one or more polypeptide molecules (or consist of multiple polypeptide subunits). Deletion of one would remedial the objection. Appropriate correction is required.

Claim Rejections - 35 USC § 112

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 23, and dependent claims 36-44 are rejected under 35 U.S.C. 112, second paragraph.

a) Claim 23 is vague and indefinite because the claim require steps for a method wherein a compound is identified for its ability to modulate the cell cycle,

however it is not clear how determining the physical, chemical or phenotypic effect on the compound reflects upon the modulation of the cell cycle. It is understandable that the cell containing the FANCA polypeptide is contacted with the test compound in order to identify a modulator, however the step of assaying chemical or phenotypic effects does not seem to correspond with identifying the compound. Applicants are requested to clarify the method. Accordingly, the metes and the bounds cannot be determined.

b) Claim 23 is vague and indefinite in the recitation, "... modulates cell cycle arrest". It is not clear from the claim how the cell cycle arrest is changed. Is the cycle arrest eliminated and allowed to proceed or altered in some form. The metes and bounds cannot be determined.

c) Claims 36-38 and 42 recite the limitation "chemical or phenotypic effect" in line 1 of claim 36, 38, and 42 and line 2 of claim 37. There is insufficient antecedent basis for this limitation in the claim. In the amended claim 23, Applicant has cancelled the active step involving "determining the chemical or phenotypic effect" therefore any depending claims cannot refer back to that active step.

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

a) Claims 23 and dependent claims 36-44 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claims(s) contains subject matter which was not described in the specification in such a way as to

enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

In making a determination as to whether an application has met the requirements for enablement under 35 U.S.C. 112 ¶ 1, the courts have put forth a series of factors. See, In re Wands, 8 USPQ2d 1400, at 1404 (CAFC 1988); and Ex Parte Forman, 230 U.S.P.Q. 546 (BPAI 1986). The factors that may be considered include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. While it is not essential that every factor be examined in detail, those factors deemed most relevant should be considered.

Applicants broadly claim a method for identifying a compound that modulates cell cycle arrest comprising contacting a cell comprising a FANCA polypeptide with 95% identity to SEQ ID NO:6 and contacting the compound with a FANCA polypeptide which is encoded by a nucleic acid 95% to SEQ ID NO:5. A polypeptide that is 95% identical to SEQ ID NO: 6 that would still maintain the function of a polypeptide that is 100% identical to SEQ ID NO:6 is unpredictable. The claims are broadly drawn to any polypeptide that is 95% identical to SEQ ID NO:6, however it is known in the art that alterations in the protein sequence can alter function. The specification teaches only SEQ ID NO:6 and does not teach whether FANCA is a member of a family of proteins

or whether FANCA can be altered and still maintain its function. Therefore the applicant is not enabled for the method of using 95% identity to SEQ ID NO:6

Protein chemistry is probably one of the most unpredictable areas of biotechnology. For example, the replacement of a single lysine at position 118 of the acidic fibroblast growth factor by a glutamic acid led to a substantial loss of heparin binding, receptor binding, and biological activity of the protein (see Burgess et al, Journal of Cell Biology Vol 111 November 1990 2129-2138). In transforming growth factor alpha, replacement of aspartic acid at position 47 with asparagine, did not affect biological activity while the replacement with serine or glutamic acid sharply reduced the biological activity of the mitogen (see Lazar et al Molecular and Cellular Biology Mar 1988 Vol 8 No 3 1247-1252).

Replacement of the histidine at position 10 of the B-chain of human insulin with aspartic acid converts the molecule into a superagonist with 5 times the activity of nature human insulin (Schwartz et al, Proc Natl Acad Sci 1987). Removal of the amino terminal histidine of glucagon substantially decreases the ability of the molecule to bind to its receptor and activate adenylate cyclase (Lin et al Biochemistry 1975).

These references demonstrate that even a single amino acid substitution or what appears to be an inconsequential chemical modification, will often dramatically affect the biological activity of the protein.

Although biotechnology has made great strides in the recent past, these references serve to demonstrate exactly how little we really know about the art. Elucidation off the genetic code induces one to believe that one can readily obtain a

functional synthetic protein for any known nucleic acid sequence with predictable results. The results of the construction of synthetic proteins remain very unpredictable as Burgess et al, Lazar et al, Schwartz et al, Lin et al conclusively demonstrate.

In addition, the art does not recognize a direct role for normally expressed FANCA protein in cell cycle arrest. The specification provides no working examples to support the Applicant's claim that a compound which physically effects (binds to) FANCA does modulate cell cycle arrest. The specification also does not provide adequate guidance on how to perform the assay and no working example showing that a compound which physically effects FANCA does in fact modulate cell cycle arrest.

In view of the lack of predictability, lack of guidance and lack of examples associated with regard to producing and using the myriad of derivatives encompassed in the scope of the claims, one skilled in the art would be forced into undue experimentation in order to practice the broadly claimed invention.

b) Claims 23, and dependent claims 36-44 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicants claim a method for identifying a compound that modulates cell cycle arrest comprising contacting a cell comprising a FANCA polypeptide with 95% identity to SEQ ID NO:6 and contacting the compound with a FANCA polypeptide which is

encoded by a nucleic acid comprising an amino acid sequence of 95% identity to SEQ ID NO: 5. Applicants specification does not adequately describe or evidence FANCA nucleic acids and polypeptides that are variants, alleles, mutants and homologs. Applicants seem to only be in possession of a FANCA nucleic acid and FANCA polypeptide that are identified as SEQ ID NO: 5 and SEQ ID NO: 6, respectively.

"Possession may be shown in a variety of ways including description of an actual reduction to practice, or by showing that the invention was 'ready for patenting' such as by the disclosure of drawings or structural chemical formulas that show that the invention was complete, or by describing distinguishing identifying characteristics sufficient to show that the applicant was in possession of the claimed invention", see Official Gazette, 1242 OG 172, January 30, 2001.

Vas-Cath Inc. V. Mahurkar, 19 USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116).

Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 U.S.C. 112 is severable from its enablement provision (see page 115).

The skilled artisan cannot envision the detailed structure of each and every molecule that could possibly be considered variants embraced by the term, FANCA and conception is not achieved until reduction to practice has occurred, see page 19 of the

specification. Adequate written description requires more than a mere statement that it is part of the invention and a reference to a potential method of isolating it. The product itself is required. Applicants have not fully described compounds and all the mutants and variants embraced by the term FANCA with sufficient particularity such that one skilled in the art would recognize that the Applicants had possession of the claimed invention. See Fiers v. Revel, 25 USPQ 2d 1601 at 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Lts., 18 USPQ2d 1016.

Furthermore, In The Reagents of the University of California v. Eli Lilly (43 USPQ2d 1398-1412), the court held that a generic statement, which defines a genus of nucleic acids by only their functional activity, does not provide an adequate written description of the genus. The court indicated that while Applicants are not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a representative number of DNA molecules, usually defined by a nucleotide sequence, falling within the scope of the claimed genus. At section B(1), the court states that "An adequate written description of a DNA.:.'requires a precise definition, such as by structure, formula, chemical name, or physical properties', not a mere wish or plan for obtaining the claimed chemical invention".

This is insufficient to support the generic claims as provided by the Interim Written Description Guidelines published in the June 15, 1998 Federal Register at Volume 63, Number 114, pages 32639-32645.

Claim Rejections - 35 USC § 102

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

a) Claim 23 is rejected under 35 U.S.C. 102(a) as being anticipated by Folias et al. (Human Molec. Genetics 2002) as evidence by the specification. Claim 23 is drawn to a method that has 2 active steps: (1) contacting a compound with Fanconi anemia group A protein (FANCA) polypeptide with 95% identity to SEQ ID NO:6 and (2) determining the physical effect of the compound upon the FANCA polypeptide. "Physical effect" is defined in the specifications (p. 20) as including ligand binding. Folias et al. teaches that contacting FANCA with BRCA1 results in ligand binding; therefore Folias et al. teaches the same active steps as applicant's claimed method.

b) Claim 23 is rejected under 35 U.S.C. 102(b) as being anticipated by McMahon et al. (J. of Biol. Chem. 1999) as evidence by the specification. Claim 23 is drawn to a method that has 2 active steps: (1) contacting a compound with Fanconi anemia group A protein (FANCA) polypeptide with 95% identity to SEQ ID NO:6 and (2) determining the physical effect of the compound upon the FANCA polypeptide. "Physical effect" is defined in the specifications (p. 20) as including ligand binding. McMahon et al. teaches that contacting FANCA with alpha Spectrin II results in ligand

binding; therefore McMahon et al. teaches the same active steps as applicant's claimed method.

Conclusion

9. No claim is allowed

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Meera Natarajan Ph.D. whose telephone number is 571-270-3058. The examiner can normally be reached on Monday-Thursday, 8:30AM-6:00PM, ALT. Friday. EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mary Mosher can be reached on 571-272-0906. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

MN

MARY MOSHER
SUPERVISORY PATENT EXAMINER

3-28-07